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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,760	07/17/2003	David L. Lewis	Mirus.030.09.2	9319

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MIRUS CORPORATION
505 SOUTH ROSA RD
MADISON, WI 53719

EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,760	LEWIS ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5 and 9-20* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 4 and 6-8 have been cancelled. Claim 5 has been amended. Applicant also introduced claims 10-20 as "withdrawn-new".

Claims 1-3, 5, and 9 are under examination.

2. All rejections pertaining to claims 6-8 are moot because Applicant cancelled the claims in the reply filed on 09/02/2008.

3. Upon further considerations, the rejections are withdrawn in favor of new rejections using secondary references providing a better motivation to arrive at the claimed invention:

The rejection of claims 1-3 and 9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 6, and 7 of U.S. Patent No. 5,744,335, in view of both Wolfert et al. (Bioconjugate Chem, 1999, 10: 993-100) and Leake et al. (PGPUB 2004/0224405);

The rejection of claims 1-3 and 9 are under 35 U.S.C. 103(a) as being unpatentable over Wolf et al. (US Patent 5,744,335) in view of each Wolfert et al. (Bioconjugate Chem, 1999, 10: 993-1004), Pollard et al. (J Biol Chem, 1998, 27: 7507-751, of record), and Leake et al. (PGPUB 2004/0224405).

New Rejections

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-3 and 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 6, and 7 of U.S. Patent No. 5,744,335, in view of both Boussif et al. (WO 01/59087) and Fire et al. (U.S. Patent No. 6,506,559). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

The instant claims are drawn to (i) a deliverable composition comprising an amphipathic compound, polyvinylamine and siRNA (claim 1); the amphipathic compound is a 1,4 disubstituted piperazine, wherein the substituting groups are C6 to C24 alkenes and R1 and R2 are the same (claims 2 and 3), and (ii) a process for the *in*

vitro delivering a siRNA to a mammalian cell (claims 5 and 9). The specification discloses that the amphipathic compound may be mixed with the polyvinylamine after the addition of siRNA (i.e., siRNA encapsulation by the amphipathic compound is not required for transfection) (p. 3, paragraph 0020).

The patent claims recite a process for transfecting a polynucleotide into a mammalian cell by delivering a composition comprising an amphipathic compound, a histone, and the polynucleotide, wherein encapsulation of the polynucleotide by the amphipathic compound is not required for transfection (claims 1 and 2), wherein the amphipathic compound is a 1,4 disubstituted piperazine and wherein the substituting groups are C6 to C24 alkenes (claims 6 and 7). The specification defines that R1 and R2 could be the same and the polynucleotide can be an antisense oligonucleotide (Summary of the invention, lines 54-67, column 7, lines 14-17). The patent claims do not recite polyvinylamine (PVA). Boussif et al. teach a method for introduction of antisense oligonucleotide into cells by using a composition comprising PVA and the antisense oligonucleotide (p. 4, last paragraph; p. 7, last paragraph; p. 8; p. 11, second to last paragraph; p. 12, last paragraph; p. 13; p. 21, last paragraph, p. 22). Based on these teachings, one of skill in the art would have known that PVA is suitable to deliver antisense oligonucleotides to cells and would have found obvious to modify the patent claims by substituting the histone with PVA to achieve the predictable result of delivering antisense oligonucleotides to cells. The patent claims taken with Boussif et al. do not teach siRNA. Fire et al. teach that siRNAs are more efficient than antisense oligonucleotides (column 2, lines 10-20, column 3, lines 19-34, column 5, lines 14-30).

It would have been obvious to one of skill in the art, at the time the invention was made, to modify the patent claims by using siRNA to obtain the predictable result of inhibiting gene expression with high efficiency.

Thus, application claims and the patent claims are obvious variants.

It is noted that none of the Applicant's argument pertains to the instant rejection. Similarly, the arguments and data presented in the 132 Declaration filed on 05/07/2008 do not pertain to the instant rejection.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3, 5, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boussif et al. (WO 01/59087), in view of each Wolf et al. (US Patent 5,744,335, of record), Bischoff et al. (U.S. Patent No. 6,291,423), and Fire et al. (U.S. Patent No. 6,506,559).

Boussif et al. teach a method for transfecting a mammalian cell *in vitro* by using a composition comprising an amphipathic compound, polyvinylamine and a nucleic acid such as an antisense oligonucleotide; the amphipathic compound greatly enhances transfection efficiency, i.e., facilitates oligonucleotide entry into the cell (claims 1, 5, and 9) (p. 4, last paragraph; p. 7, last paragraph; p. 8; p. 11, second to last paragraph; p. 12,

last paragraph; p. 13; p. 21, last paragraph, p. 22). Boussif et al. teach that any natural or synthetic amphiphile used in the art for transfection purposes can be employed in their method (p. 14).

Although Boussif et al. teach that any amphiphile known to enhance transfection efficiency can be used, they do not specifically teach 1,4 disubstituted piperazines, wherein the substituting groups are identical C6 to C24 alkenes (claims 2 and 3). However, at the time the invention was made, 1,4 disubstituted piperazines were well known and used in the prior art in transfection methods (see Wolf et al., column 2, lines 6-14 and 40-67; column 9, lines 60-67; column 10, lines 45-55; Bischoff et al., Abstract; column 4, Formula III, column 10, line 56 through column 11, line 14). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Boussif et al. by substituting their amphipathic compound with the 1,4 disubstituted piperazines taught by the prior art to achieve the predictable result of obtaining a composition suitable for introducing oligonucleotides into cells.

Boussif et al., Wolf et al., and Bischoff et al. teach antisense oligonucleotides and not siRNA (claims 1 and 5). Fire et al. teach that siRNAs are more efficient than antisense oligonucleotides in inhibiting the expression of target genes (column 2, lines 10-20, column 3, lines 19-34, column 5, lines 14-30). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Boussif et al., Wolf et al., and Bischoff et al. teach by substituting their antisense oligonucleotide with a siRNA to achieve the predictable result of inhibiting gene expression with high efficiency.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

It is noted that none of the Applicant's argument pertains to the instant rejection. Similarly, the arguments and data presented in the 132 Declaration filed on 05/07/2008 do not pertain to the instant rejection.

8. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Examiner, Art Unit 1633